

# EXHIBIT A

**IN THE UNITED STATES DISTRICT COURT  
FOR THE NORTHERN DISTRICT OF ILLINOIS  
EASTERN DIVISION**

**PSN ILLINOIS, LLC,  
an Illinois corporation,**

**Plaintiff,**

**vs.**

**Sigma-Aldrich Corp., EMD Biosciences  
Inc., VWR International LLC, Orbigen,  
Inc., Axxora Life Sciences, Inc.,  
Cayman Chemical Company, Inc.,  
Origene Technologies, Inc., Superarray  
Bioscience Corp., Tocris Bioscience, and  
Millipore Corp.**

**Defendants.**

**Case No.**

**COMPLAINT FOR  
PATENT INFRINGEMENT**

FILED: JULY 1, 2008

08CV3742

JUDGE PALLMEYER

MAGISTRATE JUDGE VALDEZ

TG

**DEMAND FOR JURY TRIAL**

**COMPLAINT**

1. Plaintiff, PSN ILLINOIS, LLC. ("PSN"), complains of defendants ("Defendants") as follows:

**NATURE OF LAWSUIT**

2. This is a claim for patent infringement arising under the patent laws of the United States, Title 35 of the United States Code.

**THE PARTIES**

3. PSN is an Illinois corporation with a place of business at 280 W. Adams Street, Chicago, Illinois 60604. PSN is the assignee of, and owns all rights, title and interest in and to, and has standing to sue for past, present and future infringement of: United States Patent No. 5,856,443, entitled "Molecular Cloning And Expression of G-Protein Coupled Receptors," issued on Jan. 5, 1999 ("the '443 patent") (Exhibit A); and

United States Patent No. 6,518,414B1, entitled “Molecular Cloning And Expression of G-Protein Coupled Receptors,” issued on Feb. 11, 2003 (“the ‘414 patent”) (Exhibit B) (collectively “PSN’s Patents”).

4. Defendant Sigma-Aldrich Corp. (Sigma) is a company incorporated in Delaware with a principal place of business at 3050 Spruce Street, St. Louis, MO 63103. Sigma transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

5. Defendant EMD Biosciences Inc. (EMD) is a company incorporated in New York with principal places of business at 10394 Pacific Center Court, San Diego, CA 92121, 441 Charmany Drive, Madison, WI 53719, and 480 S. Democrat Road, Gibbstown, NJ 08027. EMD transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

6. Defendant VWR International LLC (VWR) is a company incorporated in Delaware with its principal place of business at 1310 Goshen Parkway, West Chester, PA 193850. VWR transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

7. Defendant, Orbigen, Inc. (Orbigen) is a company incorporated in California with its principal place of business at 6827 Nancy Ridge Drive, San Diego, CA 92121. Orbigen transacts business and has sold to customers and/or offered for sale, in

this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

8. Defendant, Axxora Life Sciences, Inc. (Axxora) is a company incorporated in Delaware with its principal place of business at 6181 Cornerstone Court East, Suite 103, San Diego, CA 92121. Axxora transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

9. Defendant, Cayman Chemical Company Inc. (Cayman) is a company incorporated in Colorado with its principal place of business at 1180 E. Ellsworth Rd., Ann Arbor, MI 48108. Cayman transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

10. Defendant, Origene Technologies, Inc. (Origene) is a company incorporated in Delaware with its principal place of business at 6 Taft Court, Suite 300, Rockville, MD 20850. Origene transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

11. Defendant, Superarray Bioscience Corporation (Superarray) is a company incorporated in Delaware with its principal place of business at 15 Wormans Mill Court, Suite 101, Frederick MD 21701. Superarray transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

12. Defendant, Tocris Bioscience (Tocris) is a company incorporated in Delaware with its principal place of business at 16144 Westwoods Business Park, Ellisville, MO 63021. Tocris transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

13. Defendant, Millipore Corporation (Millipore) is a company incorporated in Massachusetts with its principal place of business at 290 Concord Rd. Billerica, MA 01821. Millipore transacts business and has sold to customers and/or offered for sale, in this judicial district, products and services that infringe claims of one or more of the MacLennan Patents, as discussed below.

#### **JURISDICTION AND VENUE**

14. This Court has exclusive jurisdiction over the subject matter of the Complaint under 28 U.S.C. §§ 1331 and 1338(a).

15. Venue in this judicial district is proper under 28 U.S.C. §§ 1391(b), (c), (d) and/or 1400(b).

#### **THE DEFENDANTS' ACTS OF PATENT INFRINGEMENT**

16. Defendant Sigma has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka p<sup>H218</sup> ("S1P2") that fall within the scope of claims of these patents, including the following products:

- i. S1P2 C-Terminal Blocking Peptide (Catalog # E8028);

- ii. Anti-S1P2, C-Terminal antibody produced in rabbit (Catalog # E7278);
- iii. Monoclonal Anti-S1P2, C-Terminal antibody produced in mouse (Catalog # E4767); and
- iv. Monoclonal Anti-S1P2, N-Terminal antibody produced in mouse (Catalog # E4892).

17. Defendant EMD has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $P^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including the following: Anti- EDG 5 (Ab-1) Mouse mAb (Catalog # GR44).

18. Defendant VWR has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $P^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including the following: S1P2 Receptor Antagonist (Catalog # 80017-352).

19. Defendant Orbigen has infringed claims of at least the '443 and '414 patents through, among other activities, the manufacture, use, offer for sale, sale, and/or distribution of products and service utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $P^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including these products:

- i. Rabbit Endothelial differentiation sphingolipid G-protein-coupled receptor 5 (EDG5) polyclonal antibody (Catalog # PAB-10630); and

- ii. Chicken Endothelial differentiation sphingolipid G-protein-coupled receptor 5 (EDG5) polyclonal antibody (Catalog # PAB-U0005).

20. Defendant Cayman has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and service utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $p^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including the following: JTE-013 (Catalog # 10009458).

21. Defendant Axxora has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and service utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $p^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including at least the following product corresponding to Cayman catalog: JTE-013 (Catalog # CAY-1009458).

22. Defendant Origene has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $p^{H218}$  ("S1P2") that fall within the scope of claims of these patents, including these products:

- i. Homo sapiens endothelial differentiation, sphingolipid G-protein coupled receptor, 5 (EDG5) as 10ug transfection ready DNA NM\_004230.2 (Catalog # SC117485);
- ii. HuSH 29mer shRNA Constructs against EDG5 Locus ID = 9294 (Catalog # TR313297);

- iii. ORF Clone of Homo sapiens endothelial differentiation, sphingolipid G-protein-coupled receptor, 5 (EDG5) as 10 ug transfection ready DNA NM\_004230.2 (Catalog # RC210163); and
- iv. shRNA constructs against Mus musculus Edg5 Locus ID = 14739 (Catalog # TR513284).

23. Defendant Superarray has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka p<sup>H218</sup> ("S1P2") that fall within the scope of claims of these patents, including these products:

- i. Human G-Protein-Coupled Receptor Signaling PathwayFinder™ (Catalog # PAHS-071);
- ii. RT<sup>2</sup> PCR Primer Set for Mouse EDG 5: Endothelial differentiation, sphingolipid G-protein coupled receptor, 5 (Catalog # PPM05309A);
- iii. Oglia GE Array Human G-Protein-Coupled Receptor Signaling PathwayFinder™ (Catalog # OHS-071 and EHS-071); and
- iv. SureSilencing shRNA Plasmid for Human EDG5: Endothelial differentiation, sphingolipid G-protein coupled receptor, 5 (Catalog # KHO2350G for the GFP marker or KH02350N for the Neomycin resistance marker).

24. Defendant Tocris has infringed claims of at least the '443 and '414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of



products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $p^{H218}$  (“S1P2”) that fall within the scope of claims of these patents, including at least the following product: S1P receptor antagonist, highly selective for S1P2 (EDG-5) (Catalog # 2392 JTE-013).

25. Defendant Millipore has infringed claims of at least the ‘443 and ‘414 patents through, among activities, the manufacture, use, offer for sale, sale, and/or distribution of products and services utilizing Sphingosine 1-Phosphate Receptor 2/ aka Edg 5/ aka  $p^{H218}$  (“S1P2”) that fall within the scope of claims of these patents, including these products and services:

- i. EDG5 AdenoSilence™ RNAi Virus Human (Catalog # GAL 10065-V7);
- ii. EDG5 AdenoSilence™ RNAi Virus Human (Catalog # GAL 10065-V6);
- iii. EDG5 AdenoSilence™ RNAi Virus Human (Catalog # GAL 10065-V5);
- iv. EDG5 AdenoSilence™ RNAi Kit Human (Catalog # GAL 10065);
- v. ChemiSCREEN™ S1P2 Calcium-Optimized FLIPR Cell Lines (Catalog # HTS078C);
- vi. ChemiSCREEN™ Human Recombinant S1P2 Lysophospholipid Receptor Calcium Optimized Ready to Assay™ (Catalog # HTS078F);
- vii. ChemiSCREEN™ Human Recombinant S1P2 Lysophospholipid Receptor Membrane Preparation (Catalog # HTS0078M); and

viii. GPCRProfiler Services which screens compounds on receptors including the S1P2 receptor.

26. The defendants' infringement, contributory infringement and inducement to infringe have injured and will continue to injure PSN unless and until this Court enters an injunction prohibiting further infringement and, specifically, enjoining further manufacture, use, offer for sale, sale and/or distribution of products and/or processes that fall within the scope of PSN's Patents.

**PRAYER FOR RELIEF**

WHEREFORE, PSN asks this Court to enter judgment against the defendants, and against their subsidiaries, affiliates, agents, servants, employees and all persons in active concert or participation with them, granting the following relief:

- A. An award of damages adequate to compensate PSN for the infringement of PSN's Patents that has occurred, together with prejudgment interest.
- B. Increased damages as permitted under 35 U.S.C. § 284.
- C. A finding that the case is exceptional and an award to PSN of its attorney fees and costs as provided by 35 U.S.C. § 285.
- D. A permanent injunction prohibiting further infringement, inducement and contributory infringement of PSN's Patents.
- E. Such other and further relief as this Court or a jury may deem proper and just.

**JURY DEMAND**

PSN demands a trial by jury on all issues presented in this Complaint.

FOR PSN ILLINOIS, LLC

/s/ Michael P. Mazza

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08CV3742

JUDGE PALLMEYER

MAGISTRATE JUDGE VALDEZ

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# EXHIBIT A



US005856443A

**United States Patent** [19]**MacLennan**[11] **Patent Number:** **5,856,443**[45] **Date of Patent:** **\*Jan. 5, 1999****[54] MOLECULAR CLONING AND EXPRESSION OF G-PROTEIN COUPLED RECEPTORS**[76] **Inventor:** **Alexander John MacLennan**, 7811 NW. 35th Pl., Gainesville, Fla. 32606[\*] **Notice:** The term of this patent shall not extend beyond the expiration date of Pat. No. 5,585,476.[21] **Appl. No.:** **760,936**[22] **Filed:** **Dec. 6, 1996****Related U.S. Application Data**

[63] Continuation of Ser. No. 196,989, Feb. 15, 1994, Pat. No. 5,585,476.

[51] **Int. Cl.<sup>6</sup>** ..... **C07K 14/705; C12N 15/12**[52] **U.S. Cl.** ..... **530/350; 435/69.1; 435/252.3; 435/320.1; 536/23.5**[58] **Field of Search** ..... **435/69.1, 252.3, 435/320.1; 530/350; 536/23.5****[56] References Cited****PUBLICATIONS**

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Julius, D., T.J. Livelli, T.M. Jessell, R. Axel (1989) "Ectopic Expression of the Serotonin 1c Receptor and the Triggering of Malignant Transformation" *Science* 244:1057-1062.

Julius, D., K.N. Huang, T.J. Livelli, R. Axel, T.M. Jessell (1990) "The 5HT<sub>2</sub> receptor defines a family of structurally distinct but functionally conserved serotonin receptors" *Proc. Natl. Acad. Sci. USA* 87:928-932.

MacLennan, A.J., G.D. Frantz, R.C. Weatherwax, N.J.K. Tillakaratne, A.J. Tobin (1990) "Expression of mRNAs That Encode D2 Dopamine Receptor Subtypes: Anatomical, Developmental, and Pharmacological Studies" *Molec. Cell. Neurosci.* 1:151-160.

Loh, E.Y., J.F. Elliott, S. Cwirla, L.L. Lanier, M.M. Davis (1989) "Polymerase Chain Reaction with Single-Sided Specificity: Analysis of T Cell Receptor  $\delta$  Chain" *Science* 243:217-220.

Sanger, F., S. Nicklen, A.R. Coulson (1977) "DNA sequencing with chain-terminating inhibitors" *Proc. Natl. Acad. Sci. USA* 74:5463-5467.

Chirgwin, J.M., E. Przbyla, R.J. MacDonald, W.J. Rutter (1979) "Isolation of Biologically Active Ribonucleic acid from Sources Enriched in Ribonuclease" *Biochem.* 18:5294-5299.

Okasaki et al. *Biochem. and Biophys. Comm.* 190(3):1104-1109, 15 Feb. 1993.

**Primary Examiner**—John Ulm**Attorney, Agent, or Firm**—Saliwanchik, Lloyd & Saliwanchik**[57] ABSTRACT**

The cloning and expression of two novel rat cDNAs ("H218" and "rat-edg") which encode two members ("p<sup>H218</sup>" and "p<sup>rat-edg</sup>") of the G-protein coupled receptor superfamily of proteins is described. The amino acid sequence similarity between "p<sup>H218</sup>" and "p<sup>rat-edg</sup>" suggests that they may be activated by the same endogenous ligand (s). The expression pattern of mRNA transcripts of both genes in cell lines, various rat tissues and developing rat brain suggests that they both play a role in cell proliferation and/or differentiation. The polynucleotide molecules, proteins, and antibodies of the subject invention can be used in both diagnostic and therapeutic applications.

**5 Claims, 12 Drawing Sheets**

U.S. Patent

Jan. 5, 1999

Sheet 1 of 12

5,856,443

35 -CCCCCCCCCTCGAGCACAGCCACAGTCACCAAGTCAGCCACTGGCTGTCCCGG  
GGCGCAGACGCCAAGCCACTCAGGCCAGGGCAGGACCCCTGGCCGCCCTAGCCAGTGCT  
CAGTCCCATGGCCCCGCCGCCACTGAGCC**GCACCATGG**CGGCTTATCTCAGAGTAC  
MetGlyGlyLeuTyrSerGluTyr 8

25 CTCAATCCTGAGAAGGTTTCAGGAACACTACAATTACACCAAGGAGACGCTGGACATGCAG  
LeuAsnProGluLysValGlnGluHisTyrAsnTyrThrLysGluThrLeuAspMetGln 28

85 GAGACGCCCTCCCGCAAGGTGGCTCCGCCCTTCATCATCATTTTATGCTGTGCCATCGTG  
GluThrProSerArgLysValAlaSerAlaPheIleIleLeuCysCysAlaIleVal 48

145 GTGGAGAACCTTCTGGTGCTAATCGCAGTGGCCAGGACAGCAAGTTCCACTCAGCCCATG  
ValGluAsnLeuLeuValLeuIleAlaValAlaArgAsnSerLysPheHisSerAlaMet 68

205 TACCTGTTCCTCGCAACCTGGCAGCCTCCGACCTGCTGGCAGCGCGTGGCCTTCGTGGCC  
TyrLeuPheLeuGlyAsnLeuAlaAlaSerAspLeuLeuAlaGlyValAlaPheValAla 88

265 AACACCTTGCTCTCCGGACCTGTACCCCTGTCTTAACTCCCTTGCAGTGGTTGCCCGA  
AsnThrLeuLeuSerGlyProValThrLeuSerLeuThrProLeuGlnTrpPheAlaArg 108

325 GAGGTTTCAGCCTTCATCAGCTCTCTGCTCGGTCTTCAGCCTCCTGGCCATTGCCATC  
GluGlySerAlaPheIleThrLeuSerAlaSerValPheSerLeuLeuAlaIleAlaIle 128

385 GAGAGACAAGTGGCCATCGCCAAAGTCAAGCTCTACGGCAGTGACAAAGCTGTGCAATG  
GluArgGlnValAlaIleAlaLysValLysLeuTyrGlySerAspLysSerCysArgMet 148

445 TTGATGCTCATTCGGGCCCTCTTGGCTGATATCGCTGATTCTGGGTGGCTTCCCCATCCTG  
LeuMetLeuIleGlyAlaSerTrpLeuIleSerLeuIleLeuGlyGlyLeuProIleLeu 168

505 GGCTGGAATTGCTTGACCATCTGGAGGCTTGCTCCACTGTGTGCCCTCTATGCTAAG  
GlyTrpAsnCysLeuAspHisLeuGluAlaCysSerThrValLeuProLeuTyrAlaLys 188

565 CACTATGTGCTCTCGGTGGTCCACCATCTTCTCTGTCTCATCTTACTGGCTATCGTGGCCTTG  
HisTyrValLeuCysValValThrIlePheSerValIleLeuLeuAlaIleValAlaLeu 208

FIG. 1A

U.S. Patent

Jan. 5, 1999

Sheet 2 of 12

5,856,443

625	TACGTCGGAATCTACTTCGTAGTCCGCTCAAGCCATGCGGACGTTGCTGCTCCTCAGACG	228
	TyrValArgIleTyrPheValValArgSerSerHisAla <u>AspValAlaGlyProGln</u> Thr	
685	CTGGCCCTGCTCAAGACAGTCACCATCGTACTGGGTGTTTTCATCATCTGCTGGCTGCCG	248
	LeuAlaLeuLeuLysThrValThrIleValLeuGlyValPheIleIleCysTrpLeuPro	
745	GCTTTTAGCATCCTTCTCTTAGACTCTACCTGTCCCGTCCGGCCGTCTCCTGTCTCCTCTAC	268
	AlaPheSerIleLeuLeuLeuAspSerThrCysProValArgAlaCysProValLeuTyr	
805	AAAGCCCATTTATTTCTTTGCCCTTCGCCACCCCTCAACTCTCTGCTCAACCCCTGTCTCTAT	288
	LysAlaHisTyrPhePheAlaPheAlaThrLeuAsnSerLeuLeuAsnProValIleTyr	
865	ACATGGCGTAGCCGGACCTTCGGAGGGAGGTACTGAGGCCCTGCTGTGCTGGCGGCAG	308
	ThrTrpArgSerArgAspLeuArgArgGluValLeuArgProLeuLeuCysTrpArgGln	
925	GGGAAGGGAGCAACAGGGCGCAGAGGTGGGAACCCCTGGTCACCGACTCCTGCCCTCCGC	328
	GlyLysGlyAlaThrGlyArgArgGlyGlyAsnProGlyHisArgLeuLeuProLeuArg	
985	AGCTCCAGCTCCCTGGAGAGAGGCTTGCCATATGCCCTACATCGCCCAACATTCTGGAGGC	348
	SerSerSerSerLeuGluArgGlyLeuHisMetProThrSerProThrPheLeuGluGly	
1045	AACACAGTGGTCTGAGGGAAATGTGAACCTGATCTGTAAACCAAGCCACAGAGAGAGCTCT	352
	AspThrValVal	

FIG. 1B

U.S. Patent

Jan. 5, 1999

Sheet 3 of 12

5,856,443

1105 GTGGGAGAGACCAGGTGACCTCATGTCTCCCTCAGTGCCACAGGCTCTGGAGGAACTGA  
 1165 CCACGGCTCATAGGTCAGGTGGCCAAACGGAGGCCACTGACTAATCAGATTGTAGTACTGTG  
 1225 ACTGTGGGACCATTAGGCTAGGGGACAGAGGCTCAGATTAGGGCTAGACATTT  
 1285 GCCACTTGGTACATAGGCTGCGCATCCTGTCTCTATCTTCCAGCTTCCCGGTTCC  
 1345 CTTCCTGCCCTCCTCTTAAAGGCCCTCTACATAGCCCGGCTAGAGCTTGCTG  
 1405 TGCAGACCAAGGCTGACCTGGACCTCCAGAGATAGATCAACTAACTGTGTCTCCTGAGTGCT  
 1465 GGGATTTTAAAGCCGTGTGCCCCCACACCCGGCTCCTGCCACCTTCCAGAAATCTTA  
 1525 GGCCACTTGTGAGGAACAACCTCTCCAGAGGACCAAGCCTTCTTCCCTGTCTCTCTG  
 1585 AGCCCTGAATCCACAGCTTCCCAATTTATCAACTGCTGCTTCTTCCCTTCTCTGTG  
 1545 TTCAGGGGAAACCACTGTGGGGCAGGAGGGTCTCTGGATCCCAGTTTTTATGCTCAG  
 1605 ATCTCACTGAGCACTTGTCTTATTGGGGAGCAGAGGAATCAGCTGAGGAGTGTTGGG  
 1665 CAGATGTTGAGGAGAAATTTGGGCTTCTCTGGTGAGAAACTCTAGGGGAGGCGTTGGTTAT  
 1725 TCCGTGAACCCAGCCTCTCTCCCCACGAACCTTTCACACCCCGCAGCCTTGAGCTGGATGC  
 1785 AAAGGCTGCTTTCAATTTGTCTTTGTAGTTTGTGTTTGTGTTTGTGTTTGTGTTTAAATT  
 1845 GGGACAGGATCTACGTACCCAGGCTGGCTCCGACTCACATATGTAGCCCAAGGCTGGCT  
 1905 TTGGACTTCTGACCTCCTGCTCCGCTTCTGGAGTGCAGGTATTACAAAGGTTGTACCCAC  
 1965 CACCACCACCACCACCAACAACAACAACAACACCTGTCTTGAAAACTATCATGA  
 2025 ATGACATGGTTACATAGCCTTGGGTGGCCAGGACATCCCGGATACCTTTATGGCATCT  
 2085 TCCTTGAAGGACTTTGCTAAATCCTGTGGAGAGTAGAAATCCAAATACGGTACAAACGG  
 2145 TATTTAAGTGTGTCTGTATCAGTGTGGGTCTGTGACCTCCTATCCAGTGTGGGTGC  
 2205 TGTCTGACCTCTTATGTGCACATCCGTGTCAAGACTGCTAGAGAGATGGACGGGGTGTG  
 2265 TGTGCTTGTGGGGTCTAGCCATGATCAGGCCCTCCTGGGAATTGCTGAATCATCTCTCCC  
 2325 ACACACAGACACACACCTCCGCCCTTAAAGAAATGTGTGAAAGAAAGGCTGAGGAAGGG  
 2385 AGATTTGGGAGGCAAGGAGCCAGTGGGAGTGTGCTCTCCCTCATACAGCTTCCCCAGATG  
 2445 TCCCCCTTGTGCTGGAAACCCAGAACTGGGCCAATAAACAGTTCAATTCTCTTGAAAAA  
 2505 AAA

FIG. 1C



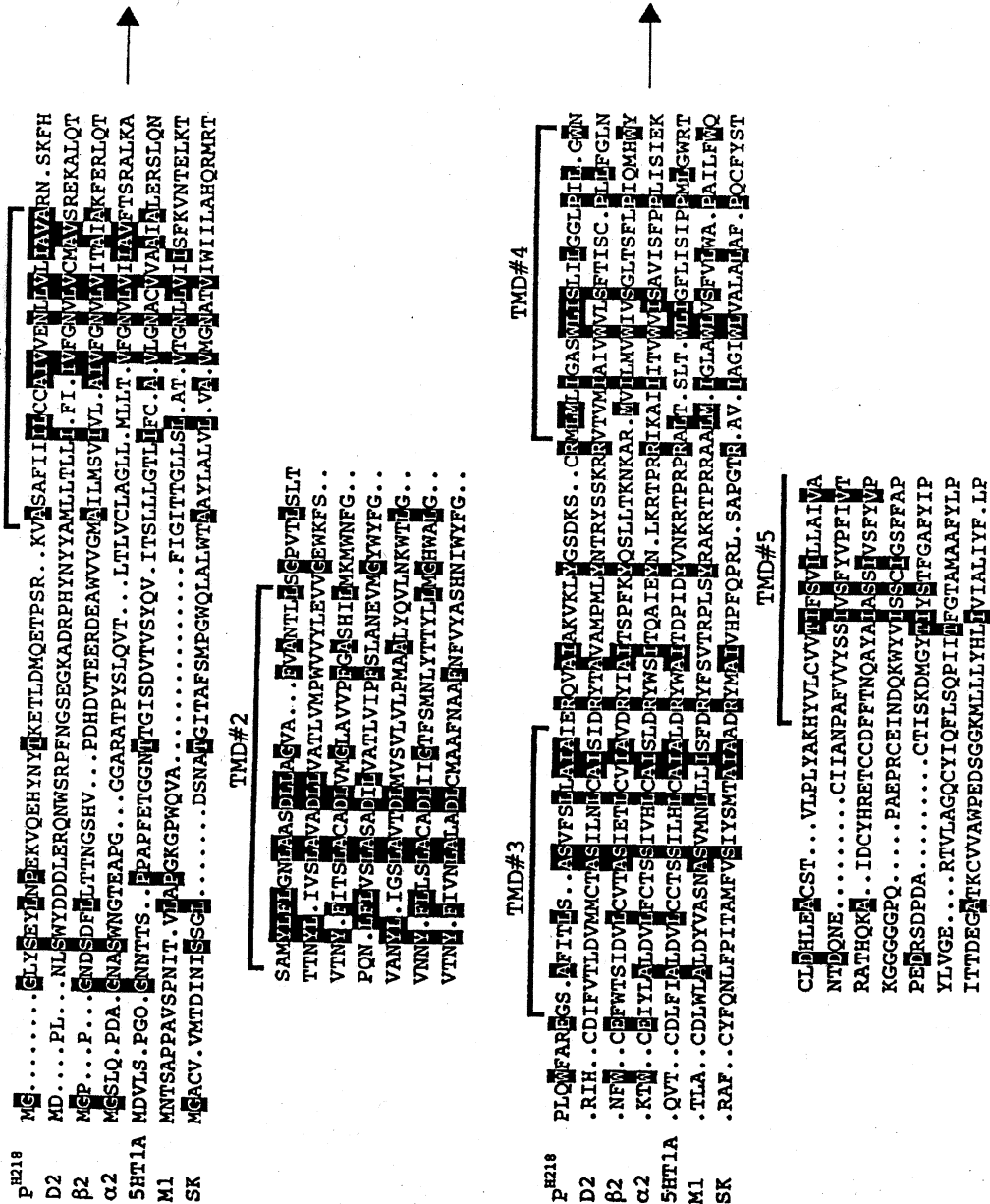
U.S. Patent

Jan. 5, 1999

Sheet 4 of 12

5,856,443

FIG. 2A



U.S. Patent

Jan. 5, 1999

Sheet 5 of 12

5,856,443

FIG. 2B

↑

TMD#6

P<sup>H218</sup> LYV..RIYFVRSSHADVAGP.....QTLALLKTVTVIVLGVFIICWLPAPFSILHLDSTCPVRACPVLY  
D2 LLVYIKIYIVLKRKRVRNTK-(112)-KEKKATQMLAIVLGVFIICWLPDEFITHILNIHC...DCNI.P  
β2 LVVMFVYSRVFQVAKRQLQK-(33)--KEHKALKTLGHIIMGIEFTLCWLPDEFIVNIVHVI...QDNLI.P  
α2 CLIMILVYVRIYQIAKRRTRV-(138)-REKRFTFVLAVVIGVFVVCWLPDEFITYTITAV...GCSV.P  
5HT1A LLLMLVLYGRIFRAARFIPK-(111)-RERKTVKTLGHIIMGTEFLCWLPDEFIVALVLPFCE.SSCHM.P  
M1 VTVMCTLYWRIYRETEENRARE-(138)-KEKKAARTLSAIIILAEFIVTWTPYNNIMVLVSTFC..KDC.V.P  
SK LVVMFVAYSIVIGLTLWRRSVP-(13)--AKKKFVKTMVLVVVTFEACWLPDEHYHLYFIIGTFQEDIYCHKFI

TMD#7

KAHY..EFAFATLNSLLNPNVYVTVWRSRDLRREVLRPILC--(46)  
PVLVSATWLGYNVNSAVNPTIYTTFNIEFRKAFMKIHH  
KEVYILLNLWLGYNVNSAFNPLIYC.RSPDFRIAFQELI.C--(37)  
RTLKFEFFWFGYCNSSLNPNVYTIENHDFRRAFKKIL.C--(8)  
TLLGAIINWLGYSNSSLNPNVYIYAYFNKDFQNAFKKIIC--(5)  
ETLWELGYWLCYVNSTINPMCYALCNKAFRDTFRLLILC--(25)  
QQVYLALEWLAMSSTMYNPIIYCCNLNHRFRSGFRLAFRC--(63)

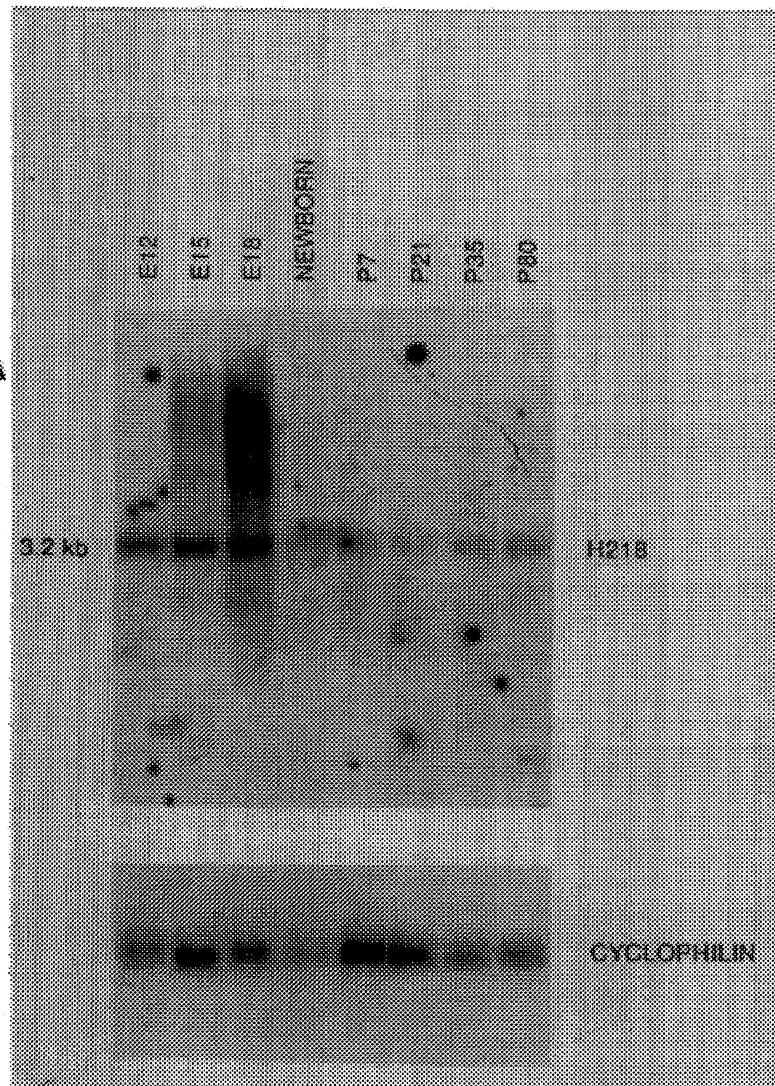
**U.S. Patent**

Jan. 5, 1999

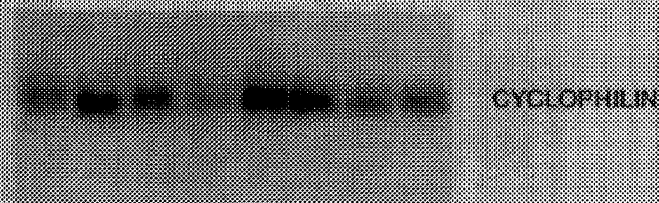
Sheet 6 of 12

**5,856,443**

**FIG. 3A**



**FIG. 3B**





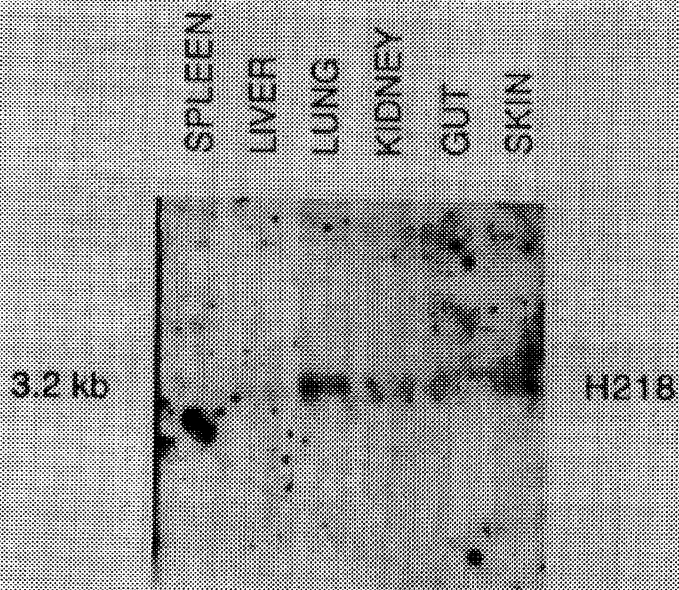
**U.S. Patent**

**Jan. 5, 1999**

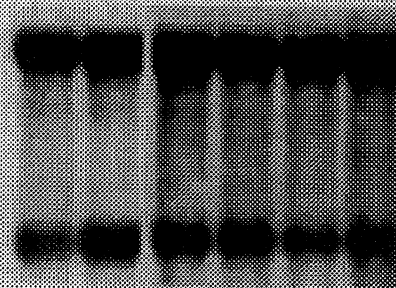
**Sheet 7 of 12**

**5,856,443**

**FIG. 4A**



**FIG. 4B**



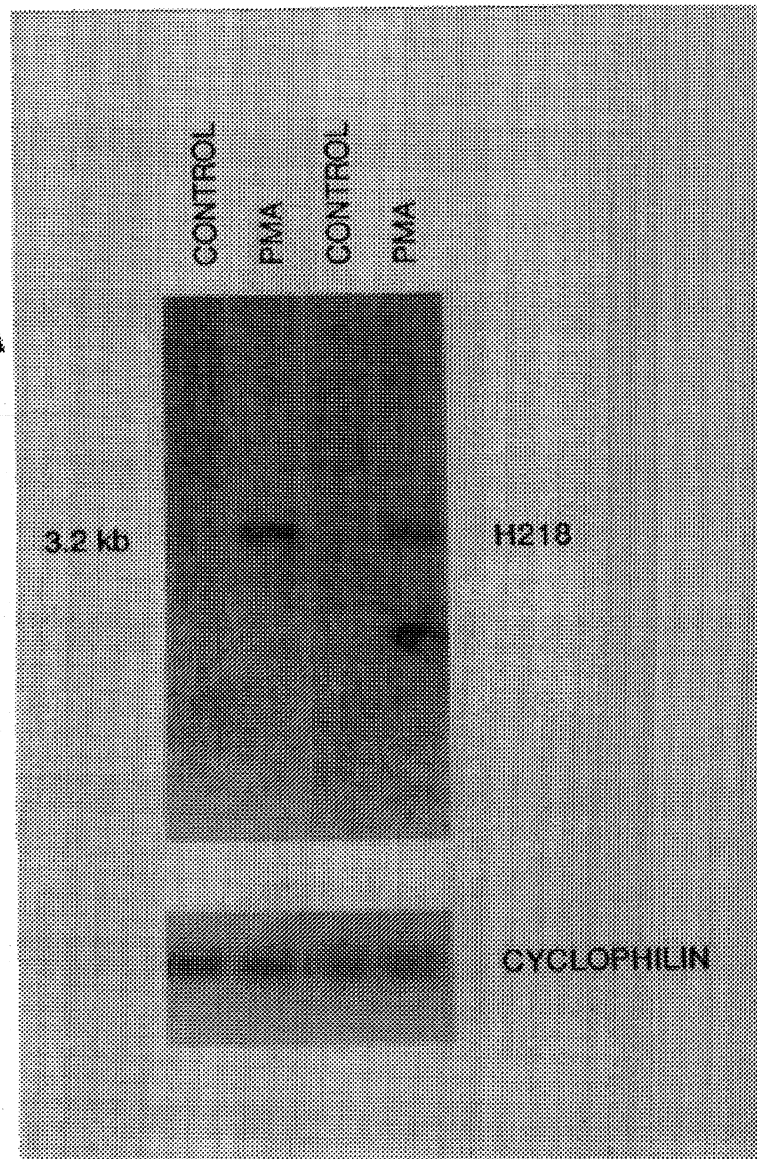
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**Jan. 5, 1999**

**Sheet 8 of 12**

**5,856,443**

**FIG. 5A**





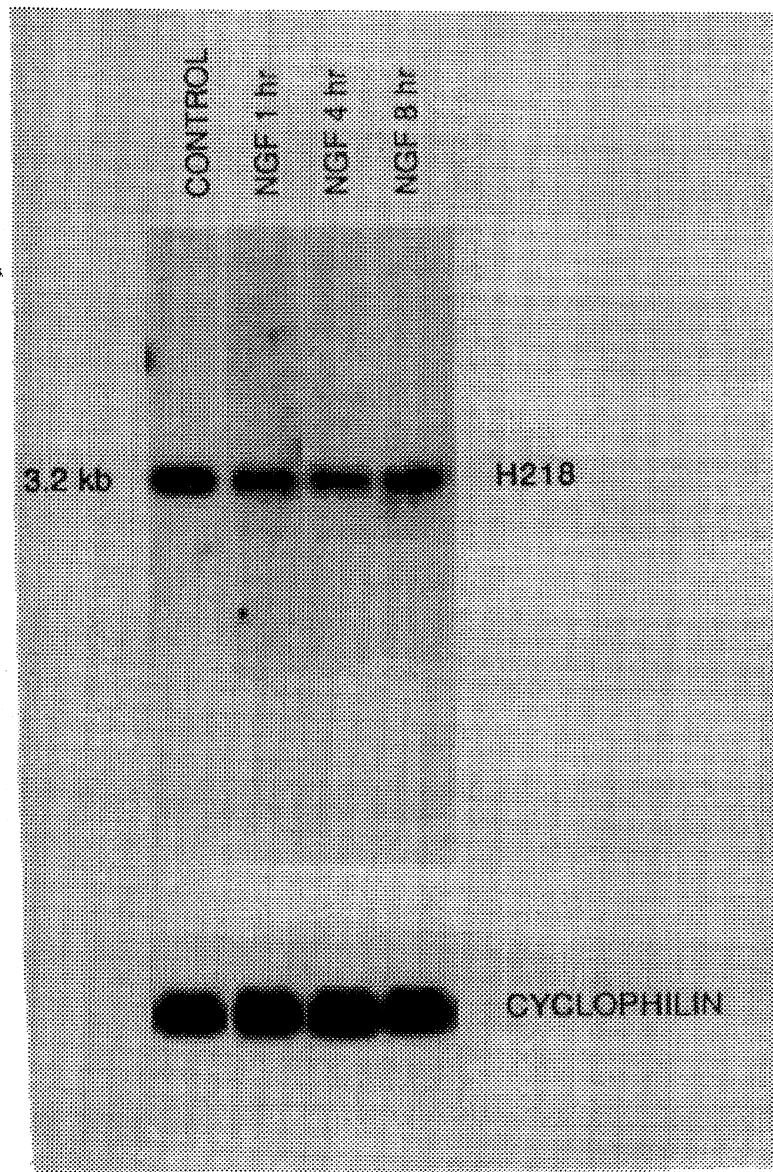
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Jan. 5, 1999

Sheet 9 of 12

**5,856,443**

**FIG. 6A**



**FIG. 6B**

CYCLOPHILIN